

CASE REPORT

Acute transverse myelitis revealing ankylosing spondylitis: A case report and literature review

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Abstract

When faced with a patient with acute myelopathy, thorough investigations should be undertaken to determine the cause. Ankylosing spondylitis should be kept in mind as a possible cause.

KEYWORDS

acute transverse myelitis, ankylosing spondylitis, spondyloarthritis

1 | INTRODUCTION

Acute transverse myelitis is a rare condition affecting patients with long-standing spondyloarthritis (SpA). However, like in the present case, this condition may precede the SpA. Physicians may therefore pay attention and screen for SpA in patients presenting with acute transverse myelitis. Spondyloarthritis (SpA) is an umbrella term applied to a group of rheumatic diseases that share common pathophysiological, genetic, and clinical features, such as the involvement of the axial skeleton, peripheral manifestations (arthritis, enthesitis, and dactylitis), and extra-articular features.¹ Radiographic axial spondyloarthritis, also known as ankylosing spondylitis (AS) is a specific subset of axial spondyloarthritis, characterized by radiographic structural changes in the sacroiliac joints. Systemic manifestations usually occur during the disease course. However, in rare cases, they can reveal the AS.²

Nervous system involvement in AS is an uncommon extra-articular feature that often affects patients with

long-standing disease.³ A wide range of neurological complications has been described including spinal cord or nerve compression as a result of atlantoaxial subluxation or vertebral fractures, cauda equina, monophasic myelopathy, and acute transverse myelitis (ATM).³

ATM is a rare, acquired focal inflammatory spinal cord dysfunction seldom described in patients with long-standing AS.⁴ We report herein a case of ATM revealing AS in a previously healthy man.

1.1 | Search strategy

We presented a case report along with the relevant literature regarding acute transverse myelitis in patients with AS. We performed a literature search in PubMed and Google Scholar using the terms: "Myelitis, Transverse" and "Spondylitis, Ankylosing" OR "Myelitis, Transverse" and "Arthritis, Psoriatic" OR "Myelitis, Transverse" and "Spondyloarthritis." The identified cases are shown in Table 1.

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2 | CASE REPORT

A 56-year-old man with a history of hypertension, visited our department for pain and numbness in the right lower limb (RLL). He did not report any family history of neurological disease. Over the past month, he developed progressive dysuria and erectile dysfunction. Clinical examination found muscular weakness of the RLL, increased lower extremity reflexes, T10 sensory level, and normal plantar reflex. The assessment of perineal sensation and anal tone did not reveal any abnormality. Sacral Thrust Test, Gaenslen test, Thrust, and Faber (or Patrick's) test were positive. The rest of the neuro-musculoskeletal examination was normal (in particular no peripheral joint involvement). Upon re-interviewing the patient, he reported inflammatory back pain for the past four months evolving since few months that was improved with non-steroidal anti-inflammatory drugs (NSAIDs).

Spinal cord magnetic resonance imaging (MRI) showed high signal intensity lesions of the central spine extending from T6 to T11 on T2-weighted images with enhancement after gadolinium. These findings were compatible with acute transverse myelitis (ATM). In addition, MRI showed Romanus lesions at the anterior vertebral corners of T7, T8, and T9, along with bone marrow edema of the sacroiliac joints (Figure 1).

Thus, the diagnosis of AS was made based on the MRI findings according to the ASAS classification criteria for axial spondyloarthritis

Laboratory examinations revealed high C-reactive protein levels (21.5mg/L), elevated erythrocyte sedimentation rate (56 mm/hour) with normal blood cell count. Serum electrolyte levels, liver, and renal function test results were normal.

We conducted several diagnostic studies in order to identify the cause of ATM. Serological testing did not indicate recent or active EBV, HSV I/II, human immunodeficiency virus, or hepatitis infection. Immunological tests including antinuclear antibodies and antineutrophil cytoplasmic antibodies were also negative. Cerebrospinal fluid (CSF) analysis showed normal cell count, protein, and glucose levels. CSF polymerase chain reactions (PCR) for *Mycobacterium tuberculosis*, Herpes simplex (HSV) I/II, cytomegalovirus, Epstein-Barr (EBV), and varicella-zoster viruses were negative. Therefore, we concluded that ATM was an AS extra-articular manifestation.

Our patient received intravenous methylprednisolone therapy (1000 mg for 3 consecutive days) with B vitaminotherapy. He was taught hygienic rules and had functional rehabilitation. Two weeks later, the patient was symptom-free. After 3 years of follow-up, his neurological status remained stable. As for the AS, he was

treated with NSAIDs (Indometacin, 150 mg/day) with good outcome.

3 | DISCUSSION

Acute transverse myelitis (ATM) is a rare, acquired focal inflammatory spinal cord dysfunction. ATM typically presents with an acute to subacute onset weakness, sensory deficits, and bowel/bladder dysfunction without involvement of cranial nerve or cerebral function.⁵

In a patient presenting with ATM, several etiologies should be considered. They can be broadly classified as para infectious process, paraneoplastic, drug or toxin-induced, systemic autoimmune disease, or acquired demyelinating disease.⁶ Several infectious agents have been suggested as potential causes of ATM including bacteria, viruses, fungi, and parasites.⁶

Our patient had no history of infection and the workup did not show any signs of infection.

Like in any spinal cord disease, MRI represents an important diagnostic tool. ATM usually shows up as focal lesions of high signal intensity on the T2-weighted image (T2WI) with contrast enhancement in the spinal cord.⁷

Acquired central nervous system autoimmune disorders including multiple sclerosis (MS), neuromyelitis optica spectrum disorder, and acute disseminated encephalomyelitis also have been reported to be associated with ATM.⁸ However, clinical presentation, brain MRI, and CSF analysis did not support this diagnosis in our patient.

ATM can also be associated with systemic inflammatory autoimmune disorder.⁹ ATM in mixed connective tissue disease is not rare, notably systemic lupus erythematosus.¹⁰ It has been also described in Sjogren syndrome,¹¹ antiphospholipid syndrome,¹² systemic sclerosis,¹³ and mixed connective tissue disease.¹⁴ These disorders have been reported as possible causes of ATM⁶

In our patient, neither clinical signs and symptoms nor auto-antibody tests supported the diagnosis of systemic autoimmune disease. However, MRI showed signs suggestive of SpA (Figure 1).

In the present case, there was no clinical nor laboratory finding indicating any disease other than AS as the cause of ATM. Thus, we considered that ATM was an extra-articular feature of AS.

Nervous system involvement in SpA is an uncommon extra-articular complication often affecting patients with long-standing disease. In a large cohort of 1,472 Brazilian patients diagnosed with SpA, only 13 (0.9%) had neurological involvement,¹⁵ the most common of which were atlantoaxial subluxation and cauda equina syndrome. The association with multiple sclerosis (MS) has been previously reported too.^{16,17} In addition, patients with SpA are

TABLE 1 Literature review: characterization of acute transverse myelitis associated with spondyloarthritis

Author publication year	Gender	Age at diagnosis of ATM (year)	SpA subtype	Disease duration of SpA (year)	Clinical presentation of ATM	Imaging	Treatment	Outcome
Lan et al (2007) ¹⁸	M	35	AS	15	Bilateral numbness along the upper limbs	NA	Methylprednisolone pulse therapy	Complete remission. But 15 years later he developed ATM, acute arachnoiditis, and cauda equina syndrome
Oh et al (2001) ⁴	M	26	AS	14	Rapid onset of motor weakness, tingling sensation in both legs, fecal incontinence.	Normal MRI	Methylprednisolone pulse therapy	Rapid improvement leading to complete clinical recovery after four weeks.
Rath et al (2010) ¹⁹	F	50	PsA	8	1-day history of rapidly ascending asymmetrical paresthesia, progressive painless weakness of the legs, urge incontinence.	A T2 hyperintense lesion of the central SC from T10 to the conus medullaris, without enhancement after gadolinium	Methylprednisolone pulse therapy	Good outcome
Sardana et al (2018) ²⁰	M	NA	AS	NA	Acute-onset quadripareisis with urinary retention	Long segment extensive spinal cord hyperintensity from C5-T1 to T3-T12 with minimal cord expansion in lower cervical and mid-lower thoracic SC	Methylprednisolone pulse therapy +long-term maintenance immunosuppressive therapy with Azathioprine	
Hwang et al (2016) ²⁶	M	31	AS	LBP for two years	Claudication of the left lower extremity, sensory impairments	Diffuse swelling of the SC and signal changes (T6-7 to T8-9)	Methylprednisolone pulse therapy	Partial improvement

Abbreviations: AS, ankylosing spondylitis; ATM, acute transverse myelitis; F, female; LBP, low back pain; M, male; NA, not available; PsA, psoriatic arthritis; SC, spinal cord; SpA, spondyloarthritis.

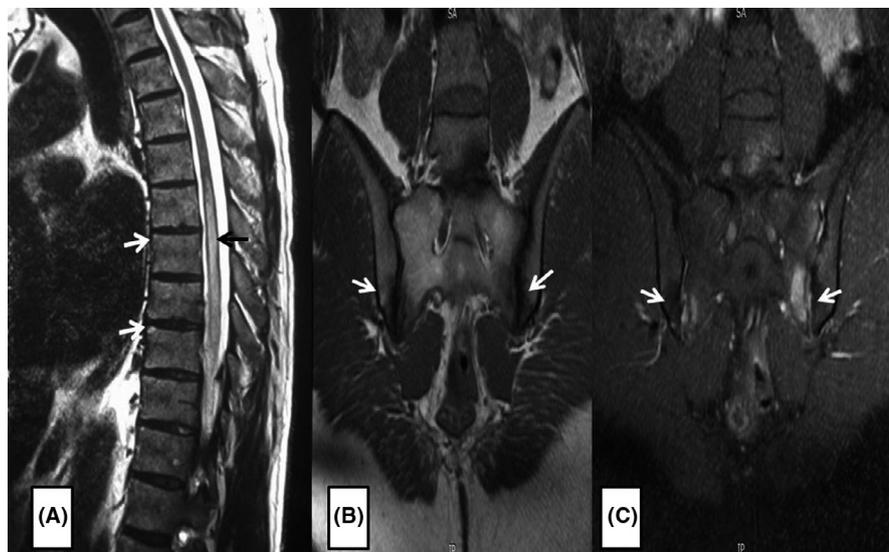


FIGURE 1 (A) MRI of the spine (T2-weighted) sagittal section showing long-segment hyperintensity involving the spinal cord extending from T6 to T11 level (black arrow) and high T2 signal of supero-anterior corners of vertebrae from T7 to T9 corresponding to Romanus lesions (white arrows). (B) MRI of the pelvis (T1-weighted) edema and erosions of the sacroiliac joints. (C) MRI of the pelvis (T1Fatsat-weighted with gadolinium) edema and erosions of the sacroiliac joints

at higher risk of vertebral fractures. ATM, however, is exceptionally rare as there are only four clearly documented cases in AS patients^{4,18} and one case in a psoriatic arthritis (PsA) patient.¹⁹

Even so, it is still unclear whether the association between ATM and AS is really underestimated or is just an accidental finding. The mechanism by which AS causes myelitis is not yet known. Several hypotheses have been suggested. The structural changes seen in the spinal canal during AS can be responsible for the bony impingement of spinal artery supplying the cord. However, in some cases, like in the present report, the MRI does not show any significant compression of the spinal cord.²⁰ Besides, spinal cord inflammation due to AS could play a role in the pathophysiology of ATM. The good response to steroids and immunosuppressive agents supports this hypothesis.

The association of multiple sclerosis and AS is more common and has received greater attention.¹⁷ Although the etiology of this association has not been fully elucidated, several hypotheses have been proposed.¹

Genetic and environmental factors play a major role in the occurrence of both diseases.

In fact, AS and MS share a genetic predisposition. It has been reported that the HLA-B7 haplotype is commonly seen in both diseases.^{21,22} A possible HLA cross-reactivity between AS and MS, especially for HLA-B27, has also been evoked.²³

Of note, the frequency of HLA-B27 ranges from 88 to 90% in AS patients,²⁴ is about 10% in MS patients controls¹⁶ and 8% of the general population worldwide.²⁵

Regarding the characteristics of AS patients with ATM, all patients but one were male.

However, unlike our patient, ATM occurred later in the course of disease. To the best of our knowledge, this is the first case of ATM revealing AS.

In the majority of reported cases, the diagnosis of AS preceded the initial symptoms of ATM from eight to 15 years.^{4,18,19,20} This suggests that ATM is rather a complication of long-standing AS. However, Hwang et al. described a patient who had experienced back pain for two years prior to the onset of ATM symptoms, but the diagnosis of AS was made at the same time as the ATM.²⁶

In the present case, the patient had experienced inflammatory low back pain during the past four months. The diagnosis of AS was made based on the findings spotted on MRI.

Although ATM, as the first manifestation of AS, is an unusual presentation, it should be considered in AS patients with neurological symptoms.

The first-line therapy for ATM is intravenous glucocorticoids pulses.^{10,14} Immunosuppressive agents such as cyclophosphamide, mycophenolate, or rituximab may be efficacious in chronic recurrent TM or resistant acute TM.⁶ Patients with acute central nervous system demyelinating disease who failed to respond to glucocorticoid therapy can benefit from plasma exchange.¹⁴ Like all the reported cases, our patient responded well to intravenous glucocorticoids pulses.

TNF-inhibitors drugs (TNFi) are new therapeutic agents that have revolutionized the management of spondyloarthritis. Although generally well tolerated, numerous studies have raised the possibility that TNFi may be responsible for central or peripheral nervous system demyelinating disorders.²⁷ The co-existence of AS and ATM has large impact on the treatment strategy since there have been few reports of patients with AS who developed ATM while being treated with TNFi.^{28,29}

Patients with AS or PsA treated with TNFi have 50% increased risk of a neuroinflammatory disease compared with those who are not.³⁰ The mechanism of demyelination associated with TNFi is yet to be determined.

Since TNF-alpha modulates the autoreactive T cells reactivity to self-antigens, its inhibition can result in an increased activity of autoreactive T cells. This phenomenon was suggested to be responsible for the autoimmune damage of the myelin sheaths.³¹

Given that TNFi can cause a decrease in immune response, the discontinuation of the treatment can result in immune reconstitution syndrome causing the autoimmune demyelination.

Thus, it seems reasonable to consider an alternative therapy other than TNFi in patients with a personal or family history of demyelinating disease.

In conclusion, when faced with a patient with an acute myelopathy, a thorough investigation should be undertaken to determine the cause. AS should be kept in mind as a possible cause of ATM and should be treated as soon as possible since it is a potential handicapping condition.

To the best of our knowledge, this is the first case report of ATM revealing an AS. In-depth studies of the pathophysiologies of these two conditions are needed to better elucidate the link between them.

CONFLICTS OF INTEREST

We declare that we have no conflict of interest.

AUTHOR CONTRIBUTIONS

Dr Soumaya Boussaid: Conceptualization, Writing—original draft, Supervision, Revision, and Validation. Dr Safa Rahmouni: Data curation, Writing—original draft, and Revision. Dr Sonia Rekik, Dr Elhem Cheour, Dr Sahli Hela, and Dr Mohamed Elleuch: Supervision and Validation. Dr Samia Jemmali: Writing—original draft.

ETHICAL APPROVAL

This study was approved by the ethical committee of la Rabta Hospital.

CONSENT

We have obtained the patient's consent for publication before inclusion in this study.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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